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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/005,642 | 12/05/2001 | Stephen T. Sonis | 50047/009002 | 8240 |

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| EXAMINER |
|---|
| BAHAR, MOJDEH |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1617 | |

DATE MAILED: 04/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. 10/005,642 | Applicant(s) SONIS, STEPHEN T. | |
|---|---|---|---|
| | Examiner Mojdeh Bahar | Art Unit 1617 | |

*-- The MAILING DATE of this communication appears on the cover sheet with th correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *24 December 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-6* is/are pending in the application.

4a) Of the above claim(s) *2, 5, 4 and 6 ( in part)* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3, 4 and 6 ( in part)* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

## DETAILED ACTION

Applicant's amendment and response to the office action of 06/19/02 submitted December 24, 2002 is acknowledged. Applicant's arguments are persuasive to remove the rejection under 35 USC 102 in the previous office action.

Newly submitted claims 2, 4 and 6 (both in part in so far as it depends from claim 2), and 5 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: These claims are drawn to methods employing an immunosuppressive agent and a TNF-alpha antagonist. The newly submitted method and the method under examination are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions have different modes of operation.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 2, 4 and 6 (both in part in so far as they depend from claim 2), and 5 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims 1, 3, 4 and 6 (both in part in so far as they depend from claim 1) are herein examined on the merits.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1, 1, 3, 4 and 6 (both in part in so far as they depend from claim 1) are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for "Decadron, triamcimalone" and "PTX and thalidomide", does not reasonably provide enablement for all "steroids" or all "TNF-alpha inhibitors". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,

2) the amount of direction or guidance provided,

3) the presence of absence of working examples,

4) the nature of the invention,

5) the state of the prior art,

6) the relative skill of those in the art

7) the predictability of the art, and

8) the breadth of the claims.

Applicant fails to set forth the criteria that defines a suitable "TNF alpha antagonist", or a suitable "steroid". Additionally, Applicant fails to provide information allowing the skilled

artisan to ascertain these compounds without undue experimentation. In the instant case, only a limited number of "TNF alpha antagonist", or "steroid" examples are set forth, thereby failing to provide sufficient working examples. It is noted that these examples are neither exhaustive, nor define the class (e.g., structure) of compounds required. The pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. The instant claims read on all "TNF alpha antagonist", and "steroids", necessitating an exhaustive search for the embodiments suitable to practice the claimed invention. Applicants fail to provide information sufficient to practice the claimed invention, absent undue experimentation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 3 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Note that the claim as written is confusing since cyclosporin is not an steroid.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim 1, 3, 4 and 6 (both in part in so far as they depend from claim 1) are rejected under 35 U.S.C. 103(a) as being unpatentable over Andrulis et al. (USPN 5,654,312) in view of Quinn et al.

Andrulis et al. (USPN 5,654,312) teaches that TNF alpha antagonists (PTX and thalidomide) and dexamethasone (glucocorticoid/corticosteroid) are useful in treating dermatoses with an autoimmune or inflammatory basis, see col. 3, line 62 to col. 4, line 55 in particular. Andrulis teaches topically applied corticosteroids are useful in treating dermatoses with an autoimmune or inflammatory basis, see col. 8, lines 13-40. Andrulis further teaches that both corticosteroids and thalidomide are known to be applied to the effected site topically in ointment form, see col. 4, lines 56-60, col. 8, lines 13-40.

Andrulis et al. (USPN 5,654,312) does not particularly teach a method of treating oral ulcerations or aphthae.

Quinn et al. teaches that aphthae is cause by an underying autoimmune mechanism, see page 4.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ TNF antagonist and steroids in the treatment of aphthae.

One of ordinary skill in the art would have been motivated to employ TNF antagonist and steroids in the treatment of aphthae because both TNF antagonist and steroids are known to be useful in treating dermatoses with an autoimmune or inflammatory basis (e.g., oral aphthae).

***Response to Arguments***

Applicant's arguments filed December 24, 2002 have been fully considered but they are not persuasive. Applicant argues that choosing the TNF antagonists and steroids suitable for the practice of this invention does not constitute undue experimentation. Note that one of ordinary skill in the art would not know which member of the class of compounds known as "TNF antagonists" and "steroids" would be suitable for the practice of this invention. Furthermore these designations cover a large number of compounds of varying structure. The skilled artisan would thus need to first conduct experimentation to find compounds that are "TNF antagonists", then combine each of these compounds with different steroids, and finally test to see which one of these combinations can be useful in the practice of this invention. This is an invitation to experiment and as such constitutes "undue experimentation."

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicant argues that the description of Andrulis would fail to indicate that the combination of thalidomide/prednisone provided any benefit over thalidomide/cyclosporin. Note that Andrulis teaches the administration of both thalidomide/prednisone and thalidomide/cyclosporin. Further Andrulis teaches that thalidomide can be topically employed along with glucocorticoids such as dextamethasone/prednisone and that each agent potentiates the effect of the other, see col. 4, lines 33-60 for example. Applicant also argues that oral

application of these combinations is not taught. Note col. 4, lines 56-60, col. 8, lines 13-40 of Andrulis where topical application to effected site is taught.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mojdeh Bahar whose telephone number is (703) 305-1007. The examiner can normally be reached on (703) 305-1007 from Monday to Friday from 9:00 a.m. to 5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, can be reached on (703) 305-1877. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Mojdeh Bahar
Patent Examiner
April 3, 2003

SREENI PADMANABHAN
PRIMARY EXAMINER

4/7/03